REMARKS

Rejections under 35 U.S.C. §112, first paragraph

The Examiner maintains the rejection of claims 1, 2, 4-6, 8, 9, 16 and 24-25 as lacking enablement under 35 U.S.C. §112, first paragraph. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

In response to Applicants arguments, the Examiner states on page 6, final paragraph, "The Examiner has provided evidence that the applicants have not enabled their claims because of their violation of the Wands factors." Applicants respectfully note that the Examiner has not provided evidence in support of her position. In addition, the Examiner has only addressed half of the eight "Wand's factors." No analysis has been provided regarding factors 2) nature of the invention 3) the state of the prior art 4) the level of ordinary skill and 7) the existence of working examples. Interestingly, three of factors that the Examiner has failed to consider are those that would require exogenous evidence. For example, factor 3 pertains to the state of the art. However, the Examiner has not addressed the state of the art. In addition, under her analysis of factor 5 the Examiner states, "the specification discloses that all of the test compounds showed

activity at a final concentration of about 10 microMoles, and that these compounds therefore are SK/IK/BK channel modulating agents. However, the specification does not go into how effective these compounds are in modulating these channels." This analysis provided by the Examiner is not relevant to the 5th Wand's factor, which is, as properly stated by the Examiner, "the level of predictability in the art." Nowhere in the analysis of the 5th Wand's factor is the predictability of the art addressed. The only comments are factual statements regarding what the specification and the disclosure thereof.

However, in the interest of facilitating the allowance of the claims, the present claims have been amended as indicated above. Nearly every substituent of the claims as amended is found in one or more of the working examples of the specification. As such, the present invention as claimed is fully enabled. No new issues for consideration have been raised by the amendments to claims since the amendments limit the claims to the scope of the dependent claims and since under M.P.E.P. §904.03 the Examiner is required to have searched the most detailed claims originally presented.

Rejections under 35 U.S.C. §112, second paragraph

Claim 1 has been rejected under 35 U.S.C. §112, second paragraph as being indefinite. More specifically, claim 1 has been rejected for the term "chemical." Claim 1 has been amended to correct the typographical error in claim 1 and to recite "chemical compound." Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §102(b)

The Examiner maintains the rejection of claims 1, 2, 4-6, 8 and 16 under 35 U.S.C. §102(b) as being anticipated by Morisawa et al. The Examiner relies on the disclosure of Preparation 2, specifically the compound diethyl(1-napthyl)methyl-(3-pyridyl)methylmalonate, as being encompassed by the present claims.

The present claims have been amended as indicated above to define the aromatic hydrocarbon groups of R^1 and R^2 as phenyl or benzyl. As such, the naphthyl derivatives of Moriwasa et al. fall outside the scope of the present claims. Withdrawal of the rejection is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD (Reg. No. 40,069) at

the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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2815-0159P

Attachment: Version with Markings to Show Changes Made

(Rev. 09/26/01)

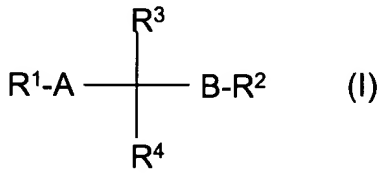
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 3, 11, 13, and 16-20 have been cancelled without prejudice or disclaimer of the subject matter contained therein.

Claims 1, 2, 4-6, 8, 9, 12 and 15 have been amended as follows.

1. (Twice Amended) A chemical compound represented by the general formula I



(I)

~~and~~ or a pharmaceutically acceptable salt ~~or an oxide~~ or a hydrate thereof,

wherein,

A and B, independently of each another represent

a group of the formula $-(CH_2)_n-$, ~~of the formula $(CH_2)_n$ Y (in either direction), or of the formula $(CH_2)_n$ Y $(CH_2)_m$ -~~,

~~in which formulas~~ wherein

n ~~and m, independently of each another, represent~~ represents 0, 1, 2, 3 or 4~~, and~~

~~Y represents O, S, or NR''', wherein R''' represents hydrogen or alkyl~~;

R^1 and R^2, independently of each another, represent alkyl, ~~alkenyl, alkynyl,~~ cycloalkyl, amino, trihalogenmethyl, nitro, cyano, or phenyl, or a group of the formula -OR', -SR', ~~-R'OR'', -R'SR'',~~ -C(O)R', -C(S)R', ~~-C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'(OR''), -C(S)NR'(OR''), -C(O)NR'(SR''), -C(S)NR'(SR''), -CH(CN)$_2$, -C(O)NR'R'', -C(S)NR'R'', -CH[C(O)R']$_2$, -CH[C(S)R']$_2$, -CH[C(O)OR']$_2$, -CH[C(S)OR']$_2$, -CH[C(O)SR']$_2$, -CH[C(S)SR']$_2$,~~ -CH_2OR', -CH_2SR', -NR'C(O)R'', or -OC(O)R';

~~an unsaturated or a partially or completely saturated mono- or polycyclic aromatic hydrocarbon group,~~ a phenyl or a benzyl group or a mono- or poly-heterocyclic aromatic group containing one or more 5- and/or 6-membered cyclic groups having one or more heteroatoms selected from the group consisting of N, O and S~~, an aryl group attached to an alkyl group; or a hetero-alkyl group having an alkyl group attached to a mono or poly heterocyclic group containing one or more heteroatoms selected from the group~~

~~consisting of N, O and S~~, wherein said ~~mono- or polycyclic~~ phenyl, benzyl or heteroaryl groups ~~or aralkyl or hetero-alkyl groups~~ are unsubstituted or are substituted one or ~~more~~ two times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, ~~alkenyl, alkynyl,~~ amino, nitro, cyano, ~~or~~ amido, ~~or~~ a group of the formula ~~-R',~~ -OR'~~,~~ and -SR', ~~-R'OR'', -R'SR'', -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', or -C(S)SR'~~, ~~or~~ a phenyl ~~or~~ and a phenoxy group~~, wherein said phenyl or phenoxy groups are unsubstituted or substituted one or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -R'OR'', -R'SR'', -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -NR'C(O)R'', or -OC(O)R'~~;

wherein

R' and R'', independently of each another, represent hydrogen, alkyl~~, alkenyl, alkynyl,~~ cycloalkyl, ~~alkoxy or phenyl,~~ or a group of the formula NR'''R'''', wherein R''' and R'''', independently of each another, represent hydrogen or alkyl;

R^3 and R^4, independently of each another, represent

~~alkyl, alkenyl, alkynyl, cycloalkyl, amino, trihalogenmethyl, nitro, cyano, or phenyl, or a group of the formula -OR', -SR', -R'OR'', R'SR'',~~ -C(O)R', ~~-C(S)R',~~ -C(O)OR', ~~-C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'(OR''), -C(S)NR'(OR''), -C(O)NR'(SR''), -C(S)NR'(SR''), -CH(CN)$_2$,~~ or -C(O)NR'R'', ~~-C(S)NR'R'', -CH[C(O)R']$_2$, -CH[C(S)R']$_2$, -CH[C(O)OR']$_2$, -CH[C(S)OR']$_2$, -CH[C(O)SR']$_2$, -CH[C(S)SR']$_2$, -CH$_2$OR', -CH$_2$SR', -NR'C(O)R'', or -OC(O)R'~~;

wherein

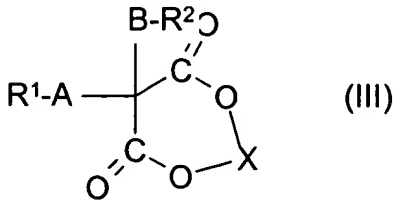
R' and R'', independently of each another, represent hydrogen, alkyl, ~~alkenyl, alkynyl,~~ cycloalkyl, ~~alkoxy or phenyl,~~ or a group of the formula NR'''R'''', wherein R''' and R'''', independently of each another, represent hydrogen or alkyl;

or R^3 and R^4 together form ~~an unsaturated or a partially or completely saturated mono- or polycyclic aromatic hydrocarbon group, or a mono- or poly-heterocyclic group, containing one or more 5- and/or 6-membered cyclic groups having one or more heteroatoms selected from the group consisting of N, O and S, wherein said mono- or polycyclic groups are unsubstituted or substituted one or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl,~~

~~alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -R'OR'', -R'SR'', -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', or -C(S)SR', or a phenyl or a phenoxy group, wherein said phenyl or phenoxy groups are unsubstituted or substituted one or more times with substituents selected from the group consisting of halogen, trihalogenmethyl, alkyl, alkenyl, alkynyl, amino, nitro, cyano, or amido, or a group of the formula -R', -OR', -SR', -R'OR'', -R'SR'', -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -NR'C(O)R'', and -OC(O)R';~~

~~wherein~~

~~R' and R'', independently of each another, represent hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy or phenyl, or a group of the formula NR'''R'''', wherein R''' and R'''', independently of each another, represent hydrogen or alkyl~~a heterocyclic 6-9 membered ring to give a diester derivative of the general formula III



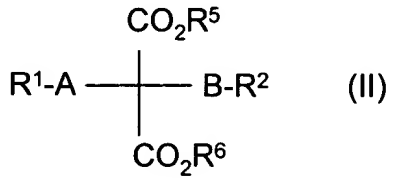
(III)

wherein

A, B, R^1 and R^2 are as defined above; and

X represents a carbon chain of the formula $-(CH_2)_n-$, wherein n is 1, 2, 3 or 4.

2. (Amended) The chemical compound according to claim 1, which is a malonic acid ester derivative of the general formula II



(II)

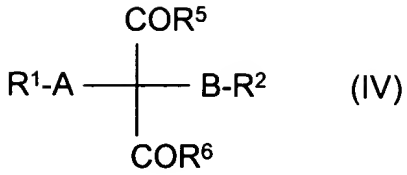
~~and~~ or a pharmaceutically acceptable salt ~~or an oxide~~ or a hydrate thereof,

wherein,

A, B, R^1 and R^2 are as defined above, and

R^5 and R^6, independently of each another, represent hydrogen, alkyl, cycloalkyl, or a group of the formula NR'''R'''', wherein R''' and R'''', independently of each another, represent hydrogen or alkyl.

4. (Amended) The chemical compound according to claim 1, which is an oxo derivative of the general formula IV



(IV)

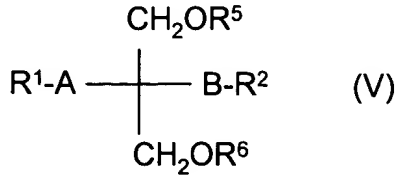
~~and~~ or a pharmaceutically acceptable salt ~~or an oxide~~ or a hydrate thereof,

wherein,

A, B, R^1 and R^2 are as defined above, and

R^5 and R^6, independently of each another, represent hydrogen, alkyl, cycloalkyl, or a group of the formula NR'''R'''', wherein R''' and R'''', independently of each another, represent hydrogen or alkyl.

5. (Amended) The chemical compound according to claim 1, which is an ether derivative of the general formula V



(V)

~~and~~ or a pharmaceutically acceptable salt ~~or an oxide~~ or a hydrate thereof,

wherein,

A, B, R^1 and R^2 are as defined above, and

R^5 and R^6, independently of each another, represent hydrogen, alkyl, cycloalkyl, or a group of the formula NR'''R'''', wherein R''' and R'''', independently of each another, represent hydrogen or alkyl.

6.(Twice Amended) The chemical compound according to any of claims 1-5, wherein R^1 and R^2 independently of each another represents a hydroxy group; an alkyl group; an alkoxy group; a group of the formula -OC(O)R' wherein R' is hydrogen or alkyl; a group of the formula -NHC(O)R'', wherein R'' is hydrogen or alkyl; a phenyl or a benzyl group, wherein said phenyl and benzyl groups are unsubstituted or substituted one or ~~more~~ two times with substituents selected from the group consisting of alkyl, alkoxy, halogen, CF_3, CN, amino, nitro, ~~or~~ and a group of the formula -NHC(O)R'', wherein R'' is hydrogen, alkyl or phenyl; a 5- or 6-membered mono- or poly-heterocyclic group, wherein said heterocyclic group is unsubstituted or substituted one or ~~more~~ two

times with substituents selected from the group consisting of halogen, CF_3, CN, amino, ~~or~~ and nitro~~; a heteroalkyl group, wherein the heterocyclic group a mono-heterocyclic group, wherein said heterocyclic group is unsubstituted or substituted one or more times with substituent selected from the group consisting of halogen, CF_3, CN, amino or nitro~~.

8. (Amended) The chemical compound according to claim 6, wherein the ~~a~~ mono-heterocyclic group is an aromatic heterocyclic monocyclic group~~, in particular~~ selected from the group consisting of 1,3,2,4- or 1,3,4,5-dioxadiazolyl, dioxatriazinyl, dioxazinyl, 1,2,3-, 1,2,4-, 1,3,2- or 1,3,4-dioxazolyl, 1,3,2,4- or 1,3,4,5-dithiadiazolyl, dithiatriazinyl, dithiazinyl, 1,2,3-dithiazolyl, furanyl, furazanyl, imidazolyl, isoimidazolyl, 2-isoimidazolyl, isoindazolyl, isothiazolyl, isoxazolyl, 1,2,3-, 1,2,4-, 1,2,5- or 1,3,4-oxadiazolyl, oxatetrazinyl, oxatriazinyl, 1,2,3,4- or 1,2,3,5-oxatriazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridinyl, pyrimidinyl, pyrrolyl (azolyl), 1,2,3,4- or 2,1,3,4-tetrazolyl, thiadiazolyl, thiazolyl, thienyl, 1,2,3-, 1,2,4- or 1,3,5-triazinyl, ~~or~~ and 1,2,3-, 1,2,4-, 2,1,3- or 4,1,2-triazolyl.

9.(Amended) The chemical compound according to claim 8, wherein the mono-heterocyclic group is selected from the group consisting of 2- or 3-furanyl, 2-, 4- or 5-imidazolyl, 3-, 4- or 5-isoxazolyl, 2-, 3- or 4-pyridinyl, ~~or~~ and 2- or 3-thienyl.

12. (Amended) The chemical compound according to claim 6, wherein the poly-heterocyclic group is ~~an aromatic heterocyclic polycyclic group, in particular~~ selected from the group consisting of acridinyl, benzimidazolyl, 1,2- or 1,4-benzisothiazinyl, 1,2- or 1,4-benzisoxazinyl, benzisoxazole, benzothiazolyl, benzofuranyl, isobenzofuranyl, 2,3-benzopyronyl, 1,2,3,4-benzotetrazinyl, 1,3,4,6-benzotetrazolyl, benzothiazolyl, 1,2,3- or 1,2,4-benzotriazinyl, 1,2,3- or 2,1,3-benzotriazolyl, benzoxadiazolyl, benzoxazolyl, carbazolyl, cinnolinyl, coumarinyl, indazolyl, indolyl, isoindolyl, indolizinyl, purinyl, phenazinyl, phenothiazinyl, phenanthridinyl, phthalazinyl, pteridinyl, quinolinyl, quinoxalinyl, isoquinolinyl, quinazolinyl, quinolizinyl, ~~or~~ and xanthrenyl.

15.(Amended) The chemical compound according to claim 1, wherein the chemical compound is

Diethyl 2-(4-fluorophenyl)-2-(3-picolyl)malonate;

Diethyl 2-(4-nitrophenyl)-2-(2-picolyl)malonate;

Diethyl 2-(4-nitrophenyl)-2-(4-picolyl)malonate;

Diethyl 2-phenyl-2-(3-picolyl)malonate;

Diethyl 2-(5-chloro-2-nitro-4-(trifluoromethyl)phenyl)-2-(3-picolyl)malonate;

Diethyl 2-benzyl-2-(3-picolyl)malonate;

Diethyl 2-(4-nitrophenyl)-2-[(benzotriazol-1-yl)methyl]malonate;

Diethyl 2-(2-thienyl)-2-(2-picolyl)malonate;

Diethyl 2-(4-(acetylamino)phenyl)-2-(2-picolyl)malonate;

Diethyl 2-(4-(benzoylamino)phenyl)-2-(2-picolyl)malonate;

2-(4-nitrophenyl)-2-(2-picolyl)malononitril;

Diethyl 2-(2-thienyl)-2-(4-nitrophenyl)malonate;

Diethyl 2-(2-thienyl)-2-(3,5-dimethylisoxazol-4-ylmethyl)malonate;

Diethyl 2-(2-thienyl)-2-(2-chlorobenzyl)malonate;

Dimethyl 2-methoxy-2-(2-picolyl)malonate;

Diethyl 2-acetamido-2-(2-picolyl)malonate;

Diethyl 2-acetamido-2-(2-chlorobenzyl)malonate;

Diethyl 2-acetamido-2-(3-chlorobenzyl)malonate;

Diethyl 2-(4-nitrophenyl)-2-(3,5-dimethylisoxazol-4-ylmethyl)malonate;

Diethyl 2-(4-nitrophenyl)-2-(benzotriazol-1-ylmethyl)malonate;

Diethyl 2-(p-tolyl)-2-(2-picolyl)malonate;

Diethyl 2-(2-thienyl)-2-(2-picolyl)malonate;

Diethyl 2-(2-chlorophenyl)-2-(2-picolyl)malonate;

Diethyl 2-(2-bromobenzyl)-2-(4-nitrophenyl)malonate;

Di-t-butyl 2-(4-nitrophenyl)-2-(2-picolyl)malonate;

Diethyl 2-(4-fluorophenyl)-2-(2-picolyl)malonate;

Diethyl 2-(4-methoxy)-2-(2-picolyl)malonate;

Diethyl 2-(4-nitrophenyl)malonate;

Diethyl 2-(5-chloro-2-nitro-4-trifluoromethylphenyl)malonate;

Diethyl 2,2-bis(2-picolyl)malonate;

Diethyl 2-(2-picolyl)malonate;

Di-t-butyl 2-(4-nitrophenyl)malonate;

Diethyl 2-phenyl-2-(acetoxymethyl)malonate;

2-Chlorophenylacetonitrile;

2-(2-Chlorophenyl)butyronitrile;

2-(2-Chlorophenyl)-2-ethylbutyronitrile;

2-(3-Phenoxyphenyl)butyronitrile;

2-Ethyl-2-(3-phenoxyphenyl)butyronitrile;

Ethyl 2-(4'-chlorophenyl))-2,2-diallyl-acetate;

Ethyl 1-(4'-chlorophenyl)cyclopent-3-ene-1-carboxylate;

Ethyl 1-(4-chlorophenyl)cyclopentane-1-carboxylate;

1-(4-Chlorophenyl)-1-(3-methyl-5-oxadiazolyl)cyclopentane;

N,N-Dimethyl 1-(4-chlorophenyl)cyclopentane-1-carboxamide;

N,N-Diethyl 1-(4-chlorophenyl)cyclopentane-1-carboxamide;

N-Phenyl 1-(4-chlorophenyl)cyclopentane-1-carboxamide;

Diethyl 2-phenyl-2-(hydroxymethyl)malonate;

Dicyclopropan(4-chlorophenyl)carbinol;

O-(2-picolyl) dicyclopropan(4-chlorophenyl)carbinol;

Diethyl 2-(2-thienyl)malonate;

Diethyl 2-(4-aminophenyl)-2-(2-picolyl)malonate;

2-(4-nitrophenyl)malononitril;

2-Cyano-2-(4-nitrophenyl)-3-(2-pyridyl)propionamide;

Diethyl 2-(4-(benzoylamino)phenyl)-2-(2-picolyl)malonate;

Diethyl 2-(4-(acetylamino)phenyl)-2-(2-picolyl)malonate;

Diethyl 2-(2-chlorophenyl)malonate;

Diethyl 2-(4-fluorophenyl)malonate;

Diethyl 2-(4-methoxyphenyl)malonate;

Diethyl 2-bromobenzylmalonate; or

Diethyl 4-chlorobenzylidenemalonate;

or a pharmaceutically acceptable salt ~~or an oxide~~ or a hydrate thereof.